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RESPIRATION AND THE AIRWAY

Rapid sequence induction and intubation with rocuronium–sugammadex compared with succinylcholine: a randomized trial

M. K. Sørensen[1]*, C. Bretlau[2], M. R. Gätke[2], A. M. Sørensen[1] and L. S. Rasmussen[1]

[1] Department of Anaesthesia, Centre of Head and Orthopaedics, Copenhagen University Hospital, Rigshospitalet, Blegdamsvej 9, 2100 Copenhagen, Denmark
[2] Department of Anaesthesiology, Copenhagen University Hospital, Herlev Hospital, Herlev Ringvej 75, 2730 Herlev, Denmark
* Corresponding author. E-mail: martin@kryspin.dk

Editor's key points

- Succinylcholine is recommended for rapid sequence induction because of its quick onset and offset of actions.
- The offset of action of succinylcholine was compared with that of the rocuronium–sugammadex sequence.
- Sixty-one patients were studied in a randomized and blinded manner.
- Importantly, the rocuronium–sugammadex sequence had significantly quicker offset of neuromuscular blocking agent effect compared with succinylcholine.

Background. An unanticipated difficult airway may arise during rapid sequence induction and intubation (RSII). The aim of the trial was to assess how rapidly spontaneous ventilation could be re-established after RSII. We hypothesized that the time period from tracheal intubation to spontaneous ventilation would be shorter with rocuronium–sugammadex than with succinylcholine.

Methods. This randomized and patient- and observer-blinded trial was approved by the regional Ethics Committee and the Danish Medicines Agency. We included elective surgical patients undergoing general anaesthesia for RSII using alfentanil (10 μg kg^{-1}), propofol (2 mg kg^{-1}), and either succinylcholine (1 mg kg^{-1}) or rocuronium (1 mg kg^{-1}). Sugammadex (16 mg kg^{-1}) was given in the rocuronium group after tracheal intubation. The primary endpoint was the time from correct placement of the tracheal tube to spontaneous ventilation, defined as a respiratory rate of more than 8 bpm and a tidal volume of at least 3 ml kg^{-1} for 30 s.

Results. We included 61 patients; of whom, 55 were evaluated for the primary endpoint. The median time from tracheal intubation to spontaneous ventilation was 406 s with succinylcholine and 216 s with rocuronium–sugammadex ($P = 0.002$). The median time from tracheal intubation to 90% recovery of the first twitch in train-of-four (T_1 90%) was 518 s with succinylcholine and 168 s with rocuronium–sugammadex ($P < 0.0001$). Intubation conditions and time to tracheal intubation were not significantly different.

Conclusions. RSII with rocuronium followed by reversal with sugammadex allowed earlier re-establishment of spontaneous ventilation than with succinylcholine.

Keywords: anaesthesia, intravenous; intubation, intratracheal; neuromuscular block

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Rapid sequence induction and intubation (RSII) is performed when there is an increased risk of pulmonary aspiration of gastric contents. RSII consists of the following: optimal positioning of the patient, pre-oxygenation, injection of an opioid and a hypnotic i.v., injection of a fast-acting neuromuscular blocking agent (NMBA), cricoid pressure, and tracheal intubation.[1–3]

Succinylcholine has been for a long time the NMBA of choice for RSII, because of quick onset along with excellent intubation conditions.[4] However, it has been desirable to identify an alternative to succinylcholine because of its side-effects and the risk of delayed recovery of neuromuscular function. Spontaneous recovery of a succinylcholine-induced neuromuscular block may take too long to avoid desaturation in a 'cannot intubate, cannot ventilate' situation. In some patients, the hydrolysis of succinylcholine may be severely impaired as a result of genetic or acquired low cholinesterase activity.[5 6]

As an alternative to succinylcholine, the non-depolarizing NMBA rocuronium can be used for RSII.[7] The onset time of rocuronium 1 mg kg^{-1} is around 60 s.[7] Its duration of action is, however, 122 (33) min [from injection to recovery of first twitch of train-of-four (TOF) to 75% of baseline] for a single bolus dose of 0.9 mg kg^{-1}.[8] A new antagonist, sugammadex, binds the rocuronium molecules in a 1:1 ratio [9] without having an effect on the plasma cholinesterase

or on any receptor system in the human body.[10–14] Even profound neuromuscular block with rocuronium can be quickly antagonized with sugammadex.[15]

The aim of this trial was to assess the time from verified correct tracheal tube placement after RSII until regular and spontaneous ventilation was re-established. In addition, we assessed the intubation conditions and the duration of action of NMBA using acceleromyography. We hypothesized that the time from correct tracheal tube placement to spontaneous ventilation would be shorter with rocuronium followed by sugammadex, than with succinylcholine.

Methods

The Danish Medicines Agency and the Regional Ethics Committee approved the trial, which adhered to the standards of the International Conference on Harmonization Good Clinical Practice. The trial (NCT00953550) was registered at ClinicalTrials.gov before inclusion of the first patient. Written informed consent was obtained from all patients participating in this two-centre trial.

The patients were eligible if they were between 18 and 60 yr of age and undergoing RSII. We excluded patients with known allergic reactions to propofol, alfentanil, succinylcholine, rocuronium, or sugammadex, patients undergoing emergency surgery (operation scheduled $<$24 h), a BMI of above 35 kg m^{-2}, severe renal disease defined by S-creatinine $>$0.200 mmol litre^{-1}, New York Heart Association Functional Classification above II, a Canadian Cardiovascular Society Functional Classification of Angina above II, potassium $>$5.0 mmol litre^{-1}, untreated glaucoma, neuromuscular disease, a known disposition for malignant hyperthermia, female patients of child-bearing potential, and breastfeeding women.

Trial protocol

Patients were randomized 1:1 according to a computer-generated list (GraphPad QuickCalcs, GraphPad Software®, Inc., La Jolla, CA, USA). A total of 65 sealed and opaque envelopes were prepared for the trial by staff with no other involvement in it. The Regional Ethics Committee approved inclusion until 55 assessable patients for the primary endpoint (time to re-establishment of spontaneous ventilation) were collected, with a maximum of 65 included patients. Thus, enrolment was planned to be stopped when reaching 55 patients where the primary endpoint was assessed. The intervention allocation list was securely stored without access for the investigators, along with an allocation key.

The patients were randomized to receive either succinylcholine (1 mg kg^{-1}) or rocuronium (1 mg kg^{-1}) followed by sugammadex (16 mg kg^{-1}). The investigation was timed in a logged software program TOF-Watch® SX Monitor (Version 2.5 INT 2007, Organon, The Netherlands) from the start of pre-oxygenation.

The patients were monitored with a three-lead ECG, non-invasive arterial pressure measurement, and pulse oximetry. Hypnotic depth was assessed using BIS VISTA® (Aspect Medical Systems, Inc., Norwood, MA, USA). Neuromuscular monitoring was performed with acceleromyography using the TOF-Watch SX® (MSD, Glostrup, Denmark) connected to a computer in accordance with 'Good Clinical Research Practice in Pharmacodynamic Studies of Neuromuscular Blocking Agents II'.[16] The study arm was immobilized and the skin was cleansed before two paediatric electrodes (Cleartrode™, Conmed, Utica, NY, USA) were placed 3–6 cm apart over the ulnar nerve near the wrist. With Hand Adaptor® (MSD), a small preload was placed on the thumb for monitoring acceleration. After induction of anaesthesia, supramaximal stimulation was ensured using an automated calibration (CAL2). Every 15 s, a TOF pattern was delivered. The neuromuscular monitoring was performed until recovery of twitch responses in TOF had reached a plateau that was maintained for at least 2 min. A re-calibration was performed after ensuring that the first twitch (T_1) in TOF had reached the plateau. The plateau was defined as: little or no further increase in T_1-amplitude. The re-calibration was followed by TOF stimulation of at least three measurements with $<$5% variation in T_1 values. Measurements were discarded if they did not acquire this stable plateau. We also discarded measurements that did not reach $<$95% depression in T_1 after injection of succinylcholine. The palmar skin temperature was kept above 32°C and the central temperature was kept above 35°C.

The RSII procedure was conducted as described below (Fig. 1). After pre-oxygenation, alfentanil (10 μg kg^{-1}) and propofol (2 mg kg^{-1}) were given. Thereafter, propofol infusion was started. This was followed by calibration of TOF-Watch® SX and TOF nerve stimulation. Either succinylcholine (1 mg kg^{-1}) or rocuronium (1 mg kg^{-1}) was then given, followed by cricoid pressure and tracheal intubation. Upon verification of correct tracheal tube placement, sugammadex (16 mg kg^{-1}) was given to patients in the rocuronium group. Correct tracheal tube placement was confirmed by auscultation of the chest and epigastrium, visualization of thoracic movement, and the appearance of a typical capnography waveform.

Hypnotic level was kept in bispectral index (BIS) target range of 45–55 with a propofol infusion, starting at 3 mg kg^{-1} h^{-1}. Additional small bolus doses of propofol were given as required to maintain BIS within the target range. End-tidal P_{CO_2} was targeted to just below 7.0 kPa with gentle ventilation at low frequency to avoid excessive hypercapnia and also desaturation.

The patient and the investigator evaluating the primary endpoint were blinded to the investigated drug. The investigator (in all cases, an anaesthesiology consultant) was blinded by only being allowed to enter the operating theatre after correct placement of the tracheal tube had been verified. The personnel doing the statistical evaluation were blinded to the allocation by being presented the allocation list without the key. After statistical evaluation, an abstract and a conclusion were written in two copies, one for each allocation possibility. After completion of the abstracts, the allocation key was revealed. The staff in the